Obesity and asthma – do we need expensive therapies?

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To the editor,

We read with interest the state of the art review by Umetsu on mechanisms by which obesity impacts asthma[1]. He has clearly outlined the extent to which molecular targets, both within allergic (T-helper 2 [TH2]) and non-allergic mechanistic pathways of asthma, need further evaluation and drug development for obese asthmatics. This was on the basis that current standard therapies for asthma such as inhaled corticosteroids (ICS) appear to be less effective in these individuals. Whilst these novel molecular targets are clearly an exciting step forward, we believe there are several other issues that need to be addressed as well when it comes to standard asthma treatment with ICS in the obese. Umetsu touched on altered lung mechanics in the obese stating more restriction of lung volumes[2]. We have found previously that overweight asthmatics (body mass index [BMI] ≥25kg/m^2) appear to have attenuated fractional exhaled nitric oxide (FeNO) and symptom responses as the dose of inhaled budesonide was increased up to 800µg/day compared to normal weight (BMI<25kg/m^2) counterparts receiving the same ICS dose ramp[3]. However, there were no differences seen between responses in airway calibre as measured by forced expiratory volume in 1s (FEV_1), or indeed airway hyperresponsiveness (AHR) to methacholine. Therefore, altered corticosteroid response at a molecular level alone does not necessarily explain the equal response in these latter two outcomes. Certainly, in significantly overweight individuals their lung volumes are reduced, but we did not see this difference in our cohort, presumably reflecting a modestly increased mean BMI of 30kg/m^2.

It may be, therefore, that either the ICS is not being delivered to the peripheral small airways sufficiently in obese asthmatics, in the presence of normal proximal delivery [4]. A previous study examined the effects of bariatric surgery on measures of peripheral small airway function and asthma between asthmatic and non-asthmatic obese individuals finding that the peripheral airways are more collapsible in obese asthmatics than in their non-asthmatic counterparts[5]. Indeed small airway dysfunction itself is associated with poorer asthma control[6] [7], which could feasibly have a greater impact in obese asthmatics.

Therefore, strategies to improve delivery of ICS to the peripheral airways might be a more cost-effective first step for certain obese asthmatics than going directly to more expensive biological therapies to improve their asthma control. We believe further prospective study is required into the lung distribution and clinical utility of extra-fine particle ICS in obese asthmatics, as well to establish if higher than usual doses of ICS are required to achieve the same effect as in normal weight asthmatics. It goes without saying that strategies which target significant weight loss – including bariatric surgery where necessary – are likely to be even more cost-effective in the first place, as this will not only impact on improving asthma control but also on comorbidities such as diabetes and hypertension.

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